VERSION WITH MARKINGS TO SHOW CHANGES MADE IN THE CLAIMS

The changes relative to the previous version of the rewritten claim 1 are marked up as follows.

Claim 1 (amended). A method of generating amplified messenger RNAs [with] using polymerase reaction activity, comprising the steps of:

(a) providing a plurality of intracellular messenger RNAs for following steps (b) to (f);

(b) contacting said messenger RNAs with a plurality of first oligodeoxythymidylate-containing primers to form a plurality of first-strand complementary DNAs, wherein said first-strand complementary DNAs are generated by reverse transcription of said messenger RNAs with extension of said first primers;

(c) permitting terminal extension of said first-strand complementary DNAs to form a plurality of polynucleotide-tailed first-strand complementary DNAs, wherein said polynucleotide-tailed first-strand complementary DNAs are tailed by multiple copies of deoxynucleotides;

(d) incubating denatured said polynucleotide-tailed first-strand complementary DNAs with a plurality of second primers to form a plurality of double-stranded complementary DNAs, wherein said double-stranded complementary DNAs are generated by extension of DNA polymerase activity with said second primers;

(e) permitting transcription of said double-stranded complementary DNAs to form a plurality of amplified RNAs, wherein said amplified RNAs are generated by extension of RNA polymerase activity through the promoter region of said double-stranded complementary DNAs; and

(f) contacting said amplified RNAs with said first primer sequences to form a plurality of said polynucleotide-tailed first-strand complementary DNAs, wherein said polynucleotide-tailed first-strand complementary DNAs are generated by reverse transcription of said amplified RNAs with extension of said first primer sequences.

REMARKS-General

1. The amended independent claim 1 incorporates all structural limitations of the original claim 1 and changes the preamble from "A method of generating amplified messenger RNAs with polymerase reaction activity" to --A method of generating amplified messenger RNAs using polymerase reaction activity--, so as to render the claim 1 to be of sufficient clarity and detail to enable a person of average skill in the art to make and use the instant invention, pursuant to 35 USC 112. No new matter has been included.

Response to Rejection of Claim 1-3, 7-18, 20, 22, 23, 25, 26, and 29-35 under 35USC112

2. The applicants submit that the amended claim 1 and the dependent claims 2-3, 7-18, 20, 22, 23, 25, 26, and 29-35 thereof are particularly point out and distinctly claim the subject matter of the instant invention, as pursuant to 35USC112.

Response to Rejection of Claims 1-3, 7-18, 20, 22, 23, 25, 26, and 29-35 under 35USC103(a)

3. The applicants acknowledge that the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein.

4. The Examiner rejected claims 1-3, 7-18, 20, 22, 23, 25, 26, and 29-35 under 35USC103(a) as being unpatentable over Mallet et al., in view of Van Gelder et al.

5. Mallet et al. teach a method to generate antisense RNA (aRNA) using RNA polymerases, but not sense RNA. Because most of natural messenger RNA (mRNA) contains a poly(A) oligonucleotide sequence in 3'-tail.

6. Van Gelder et al., on the other hand, use an oligo(dt)-promoter primer during reverse transcription to incorporate an RNA promoter to the 3'-poly(A)-tail site. As the promoter so obtained is located in the antisense orientation, the resulting RNA of Van Gelder's method is antisense RNA (aRNA) which is complementary to original mRNA and cannot be translated into protein.

7. The Examiner appears to reason that since Mallet et al. teach a method whereby RNA is first subjected to reverse transcription so as to generate applicant's "first-stranded complementary DNAs" These cDNAs are then incubated with primers and subjected to amplification so to yield applicants' "amplified RNAs", it would have been obvious to one skilled in the art to have modified the method of Mallet so to permit the transcription of DNA into RNA as Van Gelder et al., teach explicitly of conducting transcription of amplified cDNA. But this is clearly **not** a proper basis for combining references in making out an obviousness rejection of the present claims. Rather, the invention must be considered as a whole and there must be something in the reference that suggests the combination or the modification. See Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick, 221 U.S.P.Q. 481, 488 (Fed. Cir. 1984) ("The claimed invention must be considered as a whole, and the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination"), In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984), ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.") In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989), ("Although the Commissioner suggests that [the structure in the primary prior art reference] could readily be modified to form the [claimed] structure, "[t]he mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.")

8. In the present case, there is no such suggestion. Mallet et al. do not use sense RNA and Van Gelder et al do not teach the amplification of sense RNA or mRNA which needs to be transcribed from 5'-cap-end site. There is no homologous oligonucleotide sequence in the 5'-end of natural mRNA for promoter incorporation using the Van Gelder's method, or even in view of Mallet's method.

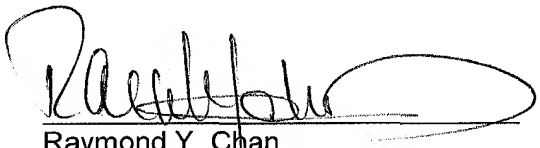
9. In any case, even combining Mallet et al. and Van Gelder et al. would not provide the invention as claimed -- a clear indicia of nonobviousness. Ex parte Schwartz, slip op. p.5 (BPA&I Appeal No. 92-2629 October 28, 1992), ("Even if we were to agree with the examiner that it would have been obvious to combine the reference teachings in the manner proposed, the resulting package still would not comprise zipper closure material that terminates short of the end of the one edge of the product containing area, as now claimed."). That is, modifying Mallet et al. with Van Gelder et al., as proposed by the

Examiner, would not generate a homologous oligonucleotide sequence in the 5'-end site by terminal transferase reaction and therefore provide an annealing site for promoter incorporation in the sense orientation. Such externally added 5'-promoter is capable of not only generating sense RNA as same as original mRNA but also assuring the full-length integrity of original mRNA. The translation-start codon for protein synthesis is usually located in the 5'-end of mRNA. The amplified RNA produced by the instant invention preserves the 5'-end of mRNA for protein synthesis.

10. Applicant believes that neither Mallet et al. nor Van Gelder et al., separately or in combination, suggest or make any mention whatsoever of the instant invention that can amplify sense mRNA which is potentially useful for protein synthesis, whereas Van Gelder et al. in view of Mallet et al. cannot do so, as recited in claim 1. The failure of providing 5'-end promoter for mRNA amplification is an unsolved problem to Van Gelder's method (publicly called aRNA amplification), even in view of Mallet's method.

11. In view of the above, it is submitted that the claims are in condition for allowance. Reconsideration and withdrawal of the objection and rejection are requested. Allowance of claims 1-3, 7-18, 20, 22, 23, 25, 26, and 19-35 at an early date is solicited.

Respectfully submitted,



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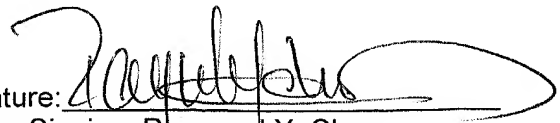
Signature: 

Person Signing: Raymond Y. Chan